REMARKS

Status of the Claims

The Applicants wish to thank the Examiner for allowing claims 20 and 21.

Claims 3, 4, 9-16 and 18-21 are pending. Claims 3, 4, 9-14, 20 and 21 were under examination. Claims 3, 4, 9, 12, 13 and 16 have been amended. Claim 22 has been added. No claims have been canceled. Therefore claims 3, 4, 9-14 and 20-22 are currently under examination. No new matter has been added.

Amendments to the Specification

Typographical errors in the specification have been corrected.

The specification has been amended to include SEQ ID numbers. The Applicants request removal of the objection to the specification on page 2 of the Action.

Amendment to the Claims

Claim 3 has been amended to remove "encoding at least two rWI2 heavy chain CDRs, selected from the group of CDRs consisting of." Support for this amendment can be found throughout the specification as filed, but at least in paragraphs [0008], [0070], [0090], [0096] and [0104] of the application as published.

Claim 4 has been amended to remove "encoding at least two rWI2 light chain CDRs, selected from the group of CDRs consisting of." Support for this amendment can be found throughout the specification as filed, but at least in paragraphs [0007], [0012], [0018], [0048], [0087] and [0104] of the application as published.

Claims 9, 12 and 13 have been amended to recite "nucleic acid sequence that encodes a" instead of "gene."

Claim 16 has been amended to correct typographical errors and to recite, "an unconjugated antibody or fragment or as a component of a conjugate, wherein an anti-idiotype antibody encoded by the nucleic acid according to claim 21 is used to clear antibody or antibody fragment that is not bound to CEA." Support for this amendment can be found throughout the specification as filed, but at least in paragraphs [0005], [0020], and [0073] of the application as published.

Claim 22 has been added. Support for this claim can be found throughout the specification as filed, but at least in paragraphs [0012], [0069], [0070], [0082], [0093], [0098] and [0104] of the application as published.

Rejection of Claims Under 35 USC 112, 2nd Paragraph

On page 3, the Action states that "[c]laims 9-14 were rejected under 35 USC 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention… [c]laims 9, 12 and 13 are indefinite for reciting "Gene." The Applicants have overcome this rejection by reciting "nucleic acid sequence that encodes a" instead of "gene." The Applicants request removal of this rejection.

Rejection of Claims Under 35 USC 112, 1st Paragraph, Enablement

Claims 3 and 4 were rejected under 35 USC 112, first paragraph for lack of enablement. The Action considers that the subject matter of claims 3 and 4 while being enabling for claiming "all of the rW12 heavy and light chain variable regions as set forth in SEQ ID NOs:1, 2 and 3 and SEQ ID NOs:4, 5 and 6 respectively, does not reasonably provide enablement for an anti-idiotype antibody which does not contain a full set of six CDRs." The Applicants respectfully traverses this rejection. However, in the interest of advancing prosecution, recitation to "at least two" light or heavy chain CDRs has been removed from the claims, which now recite, respectively, the nucleic acids of claims 20 and 21 comprising CDR-1, CDR-2 and CDR-3; or CDR1, CDR2 and CDR3.

The Applicants respectfully point out that the specification of the present application enables one skilled in the art to generate an anti-idiotype antibody or fragment thereof which contains all six CDRs or less than six CDRs. Support for these teachings can be found throughout the application but at least at paragraphs [0008], [0012], [0016] and [0052] to [0071] of the application as published. Methods known in the art such as cloning, isolating and purifying an anti-idiotype antibody or fragment thereof are disclosed.

In addition, on page 5 and 6, the Action states, "[i]t is well established that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs…" The Applicants respectfully disagree. The Action goes on to reference Rudikoff et al. (*Proc. Natl. Acad. Sci. USA* 1982, 79:1979, hereinafter "Rudikoff"). Rudikoff indicates that an IgA antibody that binds the

hapten phosphocholine A variant with decreased binding affinity was identified and isolated, S107.U4. This particular variant appears to have a somatic mutation and has decreased binding affinity to phosphocholine when it is *attached to a carrier*, or as free hapten in solution. But, Rudikoff goes on to state that many amino acid changes do not affect the antigen binding, particularly those mutations in the light chain regions of the p-CHO-binding antibodies. (Rudikoff page 1982, first column) In Rudikoff, no mutations analyzed in the light chain CDRs affected binding and it is suggested that the light chain may not be critical for association with the antigen, phosphocholine (Rudikoff, page 1981 first column). Thus, the heavy chain may be solely responsible for the interaction in this particular antigen-antibody association complex. It is clear that one amino acid change in one heavy chain region does not support the argument that all six CDRs are required for binding as stated in the Action. Conversely, Rudikoff may further support the thought that one CDR or light versus heavy chain molecules are more important for binding than another CDR(s) depending on the particular antibody and its antigenic binding site. The Applicants respectfully point out that Rudikoff fails to support the argument that all six CDRs are necessary to form functional antigen binding sites. Therefore, this reference does not apply.

In addition, the Applicants respectfully draw attention to the fact that it was, at the time of filing the present application, well known in the art that single domain antibodies which consist of a V_H or V_L domains bind specifically to antigen. Evidence for this observation of binding capacity has been recited in several publications. For example see enclosed reference Muyldermans et al, "Sequence and Structure of V_H domain from naturally occurring camel heavy chain immunoglobulins lacking light chains," *Antibody Engineering* 1994,, 7(9):1129-1135. Or see Muyldermans S., "Single domain camel antibodies: current status," *J Biotechnol* 2001, 74(4):277-302. These references were available well before the filing date of the present application and after Rudikoff.

From these documents, it is clear that V_H and V_L only antibodies are capable of binding to antigen. For at least these reasons, the Applicants consider that the recitation of the V_H or V_L only CDR sequences are sufficient to identify a functional antibody. Therefore, the assumption in the Action that the binding of the anti-idiotypic antibody requires all six CDRs is incorrect. Applicants request removal of the rejection. Applicants submit that claims 3 and 4 and 9-14 are in condition for allowance.

CONCLUSION

For the reasons stated above, Applicants submit that claims 3, 4, 9-14, and 20-22 are in condition for allowance.

Respectfully submitted,

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